



JIM GIBBONS
Governor

STATE OF NEVADA
DEPARTMENT OF HUMAN RESOURCES
DIVISION OF HEALTH CARE FINANCING AND POLICY
NEVADA MEDICAID

MICHAEL J. WILLDEN
Director

CHARLES DUARTE
Administrator

NOTICE OF OPEN PUBLIC MEETING

PHARMACY & THERAPEUTICS COMMITTEE

Las Vegas Chamber of Commerce
6671 Las Vegas Blvd. S., Suite 300
Las Vegas, NV 89119

Meeting Minutes
May 3, 2010

Committee Members Present:

Rudy Manthei, DO, Chairman
Judy Britt, Pharm.D.
David Chan, R.Ph.
Justin Holt, Pharm.D.
Michael Hautekeet, R.Ph.
Weldon Havins, MD
Constance Kalinowski, MD
Chad Luebke, Pharm.D.
Shamim Nagy, MD

Absent:

Joseph Adashek, MD

Others Present:

DHCFP: Coleen Lawrence; Chief of Program Services, Jennifer Matus; Pharmacy Program Specialist, Gabriel Lithier; Deputy Attorney General

First Health Services: Rob Coppola Pharm.D; Program Director, Dave Wuest R.Ph.; Clinical Manager, Paula Townsend Pharm.D; Clinical Manager, Shirley Hunting

Others: Sabrina Aevy-BMS, Jesse Chambers-BMS, Cris Andreson-Otsuka America Pharmaceuticals, Shannon Groppenbacher-J&J, Ester Pack-Merck, Ray Andrews-UCB, Nate Bailey-UCB, Melinda Welch-UCB, Laura Litzenberger-J&J, John Brokars-Eli Lilly, Helen Liao-Eli Lilly, Thu-Mai Dung-Sanofi-Aventis, Khanh Pham-NEAD/NV Pharmacist Association, Dana Conell-Novo Nordisk, Jannell Orr-Eli Lilly, Chris Almeida-Purdue Pharma, Larry Hinson-Astra Zeneca, Feinando Anaya-Astra Zeneca, Jen Kammerer-Astra Zeneca, Mike Soltau-Astra Zeneca, Lori Howarth-Bayer, Jesse Hong-Amylin, Anderea Wilcuts-Amylin, Gary Alling-Novo Nordisk, Bill Wauga-GSK, Irene Camerino-Forest, Jane Stephen-Allergan, Chase Freeman-Primary Care, Larry G(illegible)-Pfizer, Marilyn Semekhuk-GSK, Steve Fox-GSK, Ruben P(illegible)-GSK, Todd Phillips-GSK, Sandy Sierawski-Pfizer, Sanket Patel-Pharmacy Student, Vu Tran-Pharmacy Student, Cindy Giambrone-Novartis, Allen(illegible), Yvone Dau-Pharmacy Student, Pat Shannon-NAMI, Patti Shannon-NAMI, Irene Smith-ADA, Firhaud Ismail-Endocrinologist, Dave Spron-GSK, Ann Childress, MD-private practice, Diane Harman-Diabetes Educator, Edward Outlaw, MD-physician, Leon Ravin-SNAMNS, Domini Nal-Astra Zeneca, James Gbadebo-Pharmacy Student/USN, Lisa Durette-Child & Adult Psychiatry, Mike Gardner-Otsuka, Michael Karagiozis, DO-SNAMH, Anaray Gupta, MD-SNAMH, Corey White-Touro University, Dan Bay-Abbott, Lynn Horne-Self, Jacod Marjoaar-Self, Jen C(illegible)-Self, V. Shane Lacanienta-Pfizer.

Copies of all written testimony submitted by the public were distributed to the committee.

I. Call to Order and Roll Call

1100 E. William Street, Suite 102, Carson City, Nevada 89701
(775) 684-3600

Chairman Rudy Manthei called the meeting to order at 1:00 p.m.

II. Review and Approval of the March 25, 2010 Meeting Minutes

MOTION: Justin Holt motioned to accept the minutes as presented.
SECOND: Shamim Nagy
VOTES: Unanimous
MOTION CARRIED

III. Committee Approval of Modification of P&T Bylaws in Accordance with Statutory Changes

Coleen Lawrence stated that in accordance with Senate Bill 4 (SB4) Article V, Functions and Duties, Section I.B. has been modified with the following changes:

- Remove Section I.B.1.: Atypical and typical antipsychotic medications that are prescribed for the treatment of a mental illness of a patient who is receiving services pursuant to Medicaid;
- Remove Section I.B.3.: Anticonvulsant medications;
- Remove Section I.B.5.: Antidiabetic medications;

The P&T Committee can now discuss and take action on these classes.

MOTION: David Chan motioned to accept the proposed modifications to the P&T Bylaws as presented.
SECOND: Mike Hautekeet
VOTES: Unanimous
MOTION CARRIED

IV. DHCFFP will present legislative updates from 26th Special Legislative Session regarding Senate Bill (SB) 4

Coleen Lawrence stated that today's meeting will be addressing the drug classes discussed during the special session. She presented a review of SB4 which amended the statute governing the Nevada Medicaid Preferred Drug List.

- The bill removed the restriction from including the following drug classes on the PDL: atypical and typical antipsychotics, anticonvulsants, and the anti-diabetic classes. The P&T Committee can now discuss and take action on these classes.
- Modifications to the Medicaid Services Manual, Chapter 1200, Prescribed Drugs, based on SB4, were approved at the April 29, 2010, public hearing. The PDL exception criteria were modified to state that for atypical and typical antipsychotics, anticonvulsant and anti-diabetic medications, the recipient must demonstrate a failure of one preferred agent.
- The bill requires the following drug classes to include every therapeutic prescription drug that is classified as an anticonvulsant medication or anti-diabetic medication that is covered by Nevada Medicaid on June 30, 2010. If a therapeutic prescription drug that is included on the list of preferred prescription drugs is prescribed for a clinical indication other than the indication for which was approved as of June 30, 2010, the committee shall review the new clinical indication in accordance with regular process for new drug indications.
- The bill requires Medicaid to make available without prior authorization (PA) atypical and typical antipsychotic medications that are prescribed for the treatment of mental illness, anticonvulsant medications, and anti-diabetic medications, if the drug was prescribed before June 30, 2010, and the recipient takes the medication continuously, as prescribed on and after that date, and maintains continuous eligibility.
- The bill requires the Division of Health Care Financing and Policy to prepare a report for the legislature on the status of regulations and amounts of money saved as a result of the amended statute.

- The act becomes effective on July 1, 2010, and expires by limitation on June 30, 2011, and only applies to atypical and typical antipsychotic, anticonvulsant and anti-diabetic classes.

V. Anti-diabetic Classes:

- A. Thiazolidinediones and Combinations
- B. Alpha-Glucosidase Inhibitors
- C. Meglitinides
- D. Second Generation Sulfonylureas and Combinations
- E. Biguanides and Combinations
- F. Insulins (All)
- G. DPP IV Inhibitors and Combinations
- H. GLP-1 Receptor Agonists
- I. Amylin Analogs

1. Rob Coppola stated that in accordance with SB4, First Health Services and the Division of Health Care Financing and Policy recommends to include on the PDL every prescription drug that is currently available and classified as a anti-diabetic medication for those classes listed on the agenda as item V., classes A through I.

Dr. Manthei asked if there are any exclusions and Ms. Lawrence replied that there would be none.

Judy Britt asked if this includes all dosage forms. Ms. Lawrence replied yes, if it is covered by Medicaid under normal rules.

Ms. Lawrence clarified for the public that in accordance with SB4, DHCFP and First Health are recommending that all anti-diabetic medications available as of June 30, 2010, be included on the PDL as preferred.

2. Public Comment

Irene Smith, Nevada Chair, American Diabetes Association, asked if the preferred list that the Governor recommended for cuts would no longer be in place.

Coleen Lawrence stated that the recommendation, is that all anti-diabetic medications covered by Nevada Medicaid as of June 30, 2010, be on the preferred drug list as preferred.

Ms. Smith stated that her concern is that when the Director of Health and Human Services presented the proposal for budget cuts, he suggested that \$700,000 would be saved by using generic drugs. She felt that if this were to happen, it would be a catastrophe for the state. As a mother of two sons with Type I Diabetes, the latest medications to maintain control of diabetes are needed. She felt that whatever is prescribed by the doctor and will suit the patient should be covered and urged the committee to consider all insulins be made available.

Dave Wuest stated that all branded items in this class will be listed on the PDL as preferred.

Khanh Pham, pharmacist and certified diabetes educator, asked if insulin devices will be excluded. Her concern is that the patients she serves with uncontrolled Type II Diabetes will eventually become insulin-dependent and the devices provide accuracy and safety for her patients. Insulin pens contain pre-filled insulin.

Coleen Lawrence replied that rebateable products currently covered by Medicaid will continue to be covered. Medicaid has a diabetic supply program which the P&T does not have jurisdiction over. She offered to discuss this program with Ms. Pham at a future date and requested her contact information.

Justin Holt stated that the products Ms. Pham is referring to are different formulations of insulin packaging and not necessarily a supply. Dave Wuest added that there are currently no restrictions on the needle device.

3. Committee Discussion and Action

MOTION: Justin Holt motioned to accept DHCFP and First Health's recommendation to add all diabetic medications to the PDL.

SECOND: Judy Britt

Gabe Lither clarified for the record that this change will be effective as of July 1, 2010.

VOTES: Unanimous

MOTION CARRIED

VI. Anti-convulsant medications

A. First Generation Anticonvulsants

B. Carbamazepine Derivatives

C. Second Generation Anticonvulsants

1. Coleen Lawrence stated that in accordance with SB4, First Health Services and the Division of Health Care Financing and Policy recommends to include on the Preferred Drug List every prescription drug that is classified as an anti-convulsant medication as of June 30, 2010.

Ms. Lawrence pointed out that there was a typographical error on the agenda which is posted on the website in which VI.C.1. indicated "anti-diabetic medication". She noted that item VI. is titled "Anti-convulsant medications" and VI. A, B, and C are anti-convulsant drug classes. The corrected agenda is included in the committee's meeting packet as well as the public handouts.

Gabe Lither stated that despite the typographical error, reasonable notice was provided to the people and there is no open meeting law issue with moving forward on this item today.

2. Public Comment

No comment

3. Committee Discussion and Action

MOTION: David Chan motioned to accept the recommendation as mandated by SB4 to include all anti-convulsant medications to the PDL as of July 1, 2010.

SECOND: Shamim Nagy

VOTES: Unanimous

MOTION CARRIED

VII. Atypical and Typical Antipsychotics

Coleen Lawrence reminded the public that comment is limited to five minutes per organization.

A. Public Comment

Edward Outlaw, MD, physical medicine rehab doctor with a sub-specialty in pain, asked if the entire list of anti-convulsants will be preferred. Coleen Lawrence replied that all drugs within the class will be preferred.

Patti Shannon, NAMI, stated that she is representing herself and Joe Tyler who both suffer from mental illness and are NAMI facilitators. She understands that the legislators are trying to make atypical drugs used only as a last resort when typical drugs do not work. She is currently taking an atypical medicine that has dramatically changed her mental health for the better. For someone who is hospitalized and is prescribed an atypical drug to treat their condition that works, those drugs should be available when they are released from the hospital instead of having to go back on typical medications with side effects that are harmful to people.

Cindy Giambrone, Novartis, spoke in support of Fanapt® (iloperidone). Fanapt® is an atypical antipsychotic agent indicated for the acute treatment of schizophrenia in adults. Fanapt® is a new molecular entity which is not derived from any existing antipsychotic agents. Schizophrenia imposes a significant economic burden on the healthcare system and society exceeding 62 billion dollars annually. Seventy-four percent of patients discontinue their therapy within eighteen months as evidenced in the CATIE Trial. Extrapyramidal symptoms, metabolic effects and weight gain were the most common tolerability related reasons for discontinuation. The American Psychiatric Association and the National Association of State Mental Health Directors have both issued policy statements which conclude that no single pharmacologic approach will work for all patients and a variety of agents should be made available. The need for open access is underscored by data demonstrating negative implication of formulary restrictions on cost and quality of care. The recommended target dose for Fanapt® is 6mg-12mg administered twice daily without regard to meals. The target dose range is achieved by daily dosage adjustments to avoid orthostatic hypotension. It is recommended that responding patients be continued beyond the acute response. Fanapt® efficacy and tolerability have been proven by a number of trials and is not associated with any medically important changes in cholesterol, triglycerides, glucose or prolactin. Weight gain from baseline to endpoint was about 2.1 kilos in short and long-term studies. She referred the Committee to the package insert for warnings, precautions and complete prescribing information. She requested consideration of Fanapt® for addition to the PDL.

Lisa Durette, MD, board certified child and adolescent child psychiatrist, medical director of a private psychiatric hospital in Las Vegas, and the current president of the Nevada Psychiatric Association, spoke in support of open access of antipsychotics. She opposes restricting access based on data from eleven other states that have had restriction of medication access and have noted savings on the prescription piece but increased costs on the backend. Studies published last May demonstrated that Medicaid restrictions in ten states lead to at least 50% of patients experiencing a medication related problem via access to medication compliance with 25% of them discontinuing medications due to difficulty with access. Schizophrenic or bipolar disorder patients that become non-adherent to their medication have negative effects with increased emergency room visits. Maine's restrictive policy, which included step therapy, resulted in a 29% increased risk in medication adherence. The American Psychiatric Association's position statement is that, given the current state of knowledge, it's their opinion that the new generation of antipsychotic medications, with the exception of clozapine, need to be made available as first line treatment for appropriate individuals throughout all systems of health care and by all public and private insurers including jails, prisons and youth services facilities. The American Academy of Child and Adolescent Psychiatry has a similar statement which is to provide the optimal treatment that child and adolescent psychiatrists must have access to a full range of psychotropic medications. Complications in not having these medications impact the quality of the child's life and result in an overall increase in health care costs. The main issue of concern in Nevada is that there are very few psychiatrists per patients. Of the few that practice child and adolescent psychiatry, fewer

accept patients in the outpatient arena with Medicaid. With additional restrictions being proposed, there will be fewer psychiatrists caring for these patients. She cited examples of prior authorization restrictions with managed care Medicaid.

Dr. Manthei stated that the decisions made by the committee are not based on cost; decisions are clinically based. He asked what Dr. Durette is eluding to regarding restrictions. She responded having lack of open access to all of the psychotropic medications. Dr. Manthei asked if she is aware of anything currently being done that is restricting access when clinically necessary. Dr. Durette stated that there are none at this moment, but her understanding is that the proposal is to limit what can be prescribed to a patient.

Coleen Lawrence clarified that there is a prior authorization requirement in place for children seventeen years of age and younger for some of these classes of drugs to identify polypharmacy. Each medication must be treating a specific diagnosis.

Dr. Nagy asked how long it takes for a prior authorization to process. Ms. Lawrence replied that federal law requires a determination be made within twenty-four hours. There is also a seventy-two hour emergency fill allowed. Dr. Nagy asked if once a PA has been approved, if another PA is needed for each fill. Dave Wuest responded that PDL edits are typically granted for one year; clinical edits and length of PA approval are determined by the Drug Use Review Board (DUR).

Coleen Lawrence reminded the committee, as agendized, grandfathering will be recommended as required by SB4.

Leon Ravin, MD, board certified in general adult and forensic psychiatry, Director of Student and Resident Education-Southern Nevada Adult Mental Health Services, Clinical Associate Professor-University of Nevada School of Medicine, President-Elect-Nevada Psychiatric Association, spoke regarding the general differences in first and second generation antipsychotics. He stated that four out of five patients with psychotic disorders will relapse within the first five years and those who discontinue medications have a four or five times higher chance of relapse. Overall, patients with psychotic disorders have an adherence rate of 50%. Patients who take conventional or first generation antipsychotics are likely to have twice as many days a month of going without their medication. The mean relapse rate with first generation antipsychotics was 23% compared to the average relapse rate with the second generation drugs of 15%. He referred to the cost section of his handout.

Dr. Manthei stated that the P&T Committee is not to acknowledge the cost information.

Gabe Lither requested the handouts be collected and given to First Health as the committee, by statute, is not allowed to consider cost.

Dr. Ravin stressed that with the budget cuts, outpatient clinics and some inpatient beds have been closed. Each relapse resulted in costs significantly more than the monthly supply of medications. He stated that when he was a member for the pharmacy oversight committee, he was troubled that one of the outpatient clinics was prescribing the more expensive medications. Looking at prescribing in the different clinics over the course of ten months, it wasn't the cost of the medication prescribed to the patient, but the total amount of medication that made a difference to the patient. The clinic that was prescribing relatively cheaper medications resulted in costing more per patient.

Esther Pack, Merck, spoke in support of Saphris® (asenapine). Saphris® is indicated for the acute treatment of schizophrenia in adults and manic or mixed episodes associated with bipolar I disorder in adults. The recommended starting dosage is 10mg sublingual but can be titrated down to 5mg BID. There is no body of evidence available to answer the question of how long the bipolar or schizophrenic patient should remain on Saphris®. It is generally recommended that responding patients be continued beyond the acute

response. In August, 2009, the FDA approved asenapine; she presented data from the clinical trials and referred the committee to the AMCP dossier for a comprehensive review of the studies. Patients should be instructed to not eat or drink for ten minutes after administration of Saphris®; it is not recommended for patients with severe hepatic impairment. Dosage adjustments are not routinely required on the basis of age, gender, race or renal impairment. Class side effect profiles are similar including the black box warning that asenapine is not indicated for dementia-related psychosis in the elderly. The most common adverse reactions greater or equal to 5% in at least twice that of placebo in schizophrenia were akathisia, oral hypoesthesia and somnolence. The most common adverse reactions greater than 5% and at least twice the rate of placebo in bipolar disorder were somnolence, dizziness, extrapyramidal symptoms other than akathisia and weight increase. In studies, the mean weight gain from baseline was 0.9 kilograms. The proportion of patients with a greater or equal to 7% increase in body weight at any point was 14.7%. In the same trial, the mean change for fasting glucose was 2.4mg per deciliter; cholesterol level decreased by 6mg; fasting triglycerides went down by 9.8mg per deciliter. Atypical antipsychotics have been associated with cerebral vascular events, neuroleptic malignant syndrome, tardive dyskinesia, hyperglycemia and diabetes mellitus, syncope, leukopenia, neutropenia, and agranulocytosis, suicide and dysphagia. Asenapine is an important treatment option for patients with schizophrenia and Bipolar I Disorder. She requested the committee consider the medical and moral implication of what it would mean to deny this vulnerable and fragile group of patients a potentially life alternating treatment option. She urged the committee to place asenapine on the PDL unrestricted.

Michael Karagiozis, DO, formerly a member of the Nevada Medicaid P&T Committee, current chairman of the Pharmacy & Therapeutics Committee at Southern Nevada Adult Mental Health Psychiatric Hospital (SNAMH), introduced Dr. Anaray Gupta, Medical Director, SNAMH. Dr. Gupta stated that he is aware of the chronic non-compliance issues with patients and the concern of drugs being grandfathered in. The concern is that most patients will stop medications; once they stop medications for a period of time and need to go back on the medications that work for them, will they have to go back to the PDL list or will they be allowed to go to something not on the PDL that may work for them. The second concern is that some of the medications such as mood stabilizers, which are technically classified as anticonvulsants, will the patient be allowed to have free access to medications which, at this point are standard treatments for mood disorders in psychiatry.

Dave Wuest stated that all of the anticonvulsant agents will be preferred. Although, by policy, FDA guidelines or peer review should be followed, it is left to the clinician's judgment.

Dr. Karagiozis asked regarding grandfathering because many SNAMH patients become Medicaid patients.

Dave Wuest replied that for the anticonvulsant medications, there will be no grandfathering because all medications within the class are preferred. Patients on antipsychotic medications as of June 30, 2010, will be grandfathered.

Dr. Gupta stated that another concern is if the atypical antipsychotic is stopped and the patient has a relapse, can they go back to the medication that actually worked for them or do they have to fail a typical drug on the PDL and go through the process again.

Gabe Lither said that the statute states that the drug has to be taken continuously as prescribed.

Coleen Lawrence stated that grandfathering is typically based on claims history; i.e., if there is a history of utilization of that drug, it will be grandfathered. There are limitations. Inpatient drug data is not available in the pharmacy claims system. For non-preferred drugs, the physician would need to inform the Clinical Call Center that the

recipient is being discharged on the non-preferred medication taken during his inpatient stay in order to obtain and continue on the medication.

Judy Britt asked how far the look back is. Ms. Lawrence replied that is determined by the committee.

Dr. Karagiozis asked if this will work for the patients in the mental health system that are not yet in Medicaid. Ms. Lawrence replied that there cannot be a look back since they are not in the Medicaid system therefore a call by the physician to the call center will be required.

Dr. Manthei asked Dr. Karagiozis what his recommendation for the number of days to look back is. Dr. Karagiozis replied that the rehabilitation in this patient population is very difficult. He felt twelve to eighteen months at a minimum because patients will frequently go through three or four lapses in that period of time. The more relapses these patients have, the more expensive they are to the global cost of the system and the burden they put on society. If they are maintained in the most effective manner possible, it is easier and less costly to the system and society. These patients are chronic and they recycle.

Dr. Manthei asked how far back the data is. Ms. Lawrence replied that a look back is not more than a year since prescriptions expire a year from the date written and typically the standard is ninety days for grandfathering. The look back for antidepressants is ninety days.

Rob Coppola commented that a look back more than six months will impact the claims adjudication process in terms of how long it will take for the system to respond to a claim.

Jen Kammerer, Astra Zeneca, spoke in support of Seroquel® and Seroquel XR®. Seroquel XR® was recently FDA approved as an adjunctive treatment in adults with major depressive disorder (MDD). Approval was based on two clinical efficacy trials in adults who had MDD and had an inadequate response to at least one antidepressant. The XR formulation predominantly releases drug over the course of the day and peak plasma level is reached at six hours which offers once a day dosing for all of the approved indications. In MDD, the initial recommended dose is 50mg once a day in the evening which can be increased to 150mg per day by day three and thereafter can be adjusted within the recommended range of 150mg to 300mg per day. Seroquel® is approved for both MDD as an adjunctive therapy as well as acute depressive episodes and bipolar disorder. Seroquel® immediate release was recently approved for the treatment of schizophrenia in adolescents ages thirteen to seventeen years old as well as acute manic episodes associated with Bipolar I Disorder in children and adolescents ages ten to seventeen years old. In those indications, it is recommended that it be given twice a day and up to three times per day as needed. In the initial five day titration, the total daily recommended dose is 50mg on day one; 100mg on day two; 200mg day three; 300mg day four; 400mg day five. The recommended target ranges are 400mg - 800mg per day in schizophrenia; 400mg - 600mg per day in Bipolar I Disorder. There are no randomized controlled studies that directly compare the efficacy of Seroquel XR® to Seroquel®. The prescribing for both products contains boxed warnings. Seroquel XR® and Seroquel® are not approved for the treatment of patients with dementia related psychosis. Antidepressants increase the risk of suicidal thinking and behavior in short term studies in children, adolescents and young adults with MDD and other psychiatric disorders. Seroquel® immediate release product is not approved for use in patients under the age of ten; Seroquel XR® is not approved for use in patients under the age of eighteen years old. Both products include warning and precautions for neuroleptic malignant syndrome, hyperglycemia in diabetes, hyperlipidemia, weight gain, tardive dyskinesia, orthostatic hypotension, leucopenia, neutropenia, and agranulocytosis. The warnings and precautions also include the risk of cataracts, seizures, hypothyroidism, hyperprolactinemia, transaminase elevations, potential for cognitive and motor

impairment, priapism, body temperature regulation, dysphasia, suicide, use in patients with concomitant illness and withdrawal. The prescribing information for Seroquel® includes a warning and precaution regarding increases in blood pressure in children and adolescents. The most common adverse events associated with the use of both products in adults were somnolence, dry mouth, dizziness, constipation, increased appetite, dyspepsia, abdominal pain, fatigue, pharyngitis, lethargy, pharyngitis and nasal congestion. The most common adverse events associated with the use of Seroquel® in children and adolescent trials were somnolence, dizziness, fatigue, increased appetite, nausea, vomiting, dry mouth, tachycardia and weight gain.

Jesse Chambers, Bristol-Myers Squibb, stated that she seconds the voices that have concern for open access and the benefit for patients and caregivers. She spoke in support of aripiprazole (Abilify®). The mechanism of action is a unique molecule which functions as a dopamine 2 receptor partial agonist. No other antipsychotic on the market has this mechanism of action. Aripiprazole was invented for use in schizophrenia where it received its first indication. Subsequently, there are now fourteen indications for the medication making it the most widely indicated antipsychotic available. Seventy-five percent of prescriptions written for the medication are within those indications. Recent indications include treating irritability in autistic disorder in children six to seventeen years of age. The indication was based on two short-term trials and demonstrated benefit at doses of 5mg, 10mg and 15mg per day. The most common adverse events seen in those trials included sedation and GI disturbances. Weight gain breakdown was 0.4 kilogram for placebo group; 1.6 kilogram weight gain for aripiprazole at the end of the trial. There were no changes in metabolic parameters or prolactin. The adult indication which is based on two of three studies is adjunctive to antidepressant treatment for adults eighteen to sixty-five years of age with major depression. The most common side effect seen in trials was akathisia which occurred at a rate of one-quarter of the patients. Rates were mild to moderate; 1.3% of patients discontinued due to akathisia. No changes of clinical significance for weight or metabolic parameters were seen. Two recent trials of bipolar disorder discuss aripiprazole and the other atypical antipsychotics with the exception of clozapine in terms of hospitalization rates and total psychiatric cost. Aripiprazole demonstrated lowest hospitalization rates and lowest cost in total psychiatric medical care in comparison to the other atypicals. A similar analysis with schizophrenia looked at a utility score for utilization of atypicals. Factors were cost of the medication, adherence, efficacy and adverse events. Aripiprazole scored the highest utility value. Black box warnings include increased rate of mortality for elderly patients with dementia-related psychosis; increased risk of suicidality for children and adolescents. Aripiprazole does not have an indication for age population lower than eighteen years of age.

Ann Childress, MD, is board certified in child, adolescent and adult psychiatrist in private practice and works one day a week at Mohave Mental Health seeing seriously emotionally disturbed children. She spoke in support of continued open access without a first failure for children and adolescents. The stakes are high in adults but they are higher in kids. In five studies with risperidone over two years, prolactin tripled in several of the studies and doubled in others which mean increased gynecomastia, menstrual irregularities, and delay of puberty. Effect on bone density in kids is unknown but delaying puberty may affect an individual permanently. Weight gain may put some individuals who are within a normal weight range into the obese range. A study published in the October issue of JAMA looked at several of the atypicals in New York. In 10.8 weeks, kids four to nineteen years of age gained an average of 8.5 kilograms on olanzapine, 6 kilograms on quetiapine, 5 kilograms on risperidone and 4 kilograms on aripiprazole. The kids on quetiapine and olanzapine had significant elevations in cholesterol and triglycerides in as early as 10.5 weeks on the medication. Children on aripiprazole did not have increased metabolic parameters and their prolactin decreased. She requested if considering a first failure, children and adolescents are exempt because of their unique physiology and the effect on growth and development.

Sandy Sierawski, Pfizer, spoke in support of Geodon® and provided a brief product summary document to the committee. She stated that it's well recognized by researchers and physicians that there exist many differences among the atypical antipsychotics. The National Association of State and Mental Health Program Directors came together to adopt a set of recommendations to promote appropriate access, efficient utilization and best practice use of these medications. Among the recommendations were grandfathering and that a PDL should provide initial first-line access to a choice of antipsychotic agents that has substantial clinical differences. The evidence currently available indicates that important such differences exist in weight gain, extrapyramidal side effects, sedation and other adverse events. In head-to-head randomized controlled trials with Zyprexa® and Risperdal®, Geodon® has demonstrated equivalent efficacy but excelled in metabolic and tolerability profiles. The superiority of Geodon's® metabolic profile has been acknowledged by consensus statement from the American Psychiatric Association, American Diabetes Association, American Association of Clinical Endocrinologists and the North American Association for the Study of Obesity. Patients with schizophrenia and bipolar disorder are at two to three times increased risk of diabetes; the risk of death from a cardiovascular event is 3.5 times greater for people with metabolic syndrome than those without. Unlike several atypical antipsychotics, Geodon® is not associated with weight gain, hyperlipidemia, or elevated plasma glucose level thus potentially reducing associated risk of diabetes and coronary heart disease. In a landmark CATIE Trial comparing four atypicals and one conventional agent, all of these points were confirmed. Geodon®, when used at clinical effective doses, has demonstrated treatment persistence relative to other atypical antipsychotics. It's also been shown to be an ideal switching agent. 2009 CMS data for Nevada Medicaid payments show that Geodon® is one of the top five prescription medications in the antipsychotic class (4,500 prescriptions dispensed to Nevada Medicaid last year). Geodon® has several therapeutic benefits and proven advantages over other agents in this class. She requested that Geodon® be included on the PDL.

Robert Lynn Horne, MD, professor of psychiatry, University of Nevada School of Medicine, stated that he is appearing on behalf of himself and his patients. He suggested that the first motion that the committee makes is that all agents in this class are therapeutic alternatives not therapeutic equivalents. The first and second generation antipsychotics are not equivalent in side effects. For particular patients, the second generation antipsychotics are not equivalent in efficacy when they work fantastically in others and they have different mechanisms of action. He requested that unlimited grandfathering be granted to all patients currently on the medication for as long as it's working for them. The clinician should be able to provide the medication history to approve the medication even if the patient hasn't received a prescription for it in the past year; i.e., lifetime look back. He also requested that the committee require that a new patient fail only one antipsychotic before being able to get a non-preferred antipsychotic. Currently, only risperidone and clozapine are the atypical antipsychotics available as generic and clozapine, with its weekly blood test, is not a first or second line medication for serious medical illnesses. Don't make patients take a first generation antipsychotic before having access to non-generic second generation medications. Nevada does have the distinction of being the first state in the nation in which a psychiatrist was sued for giving a patient haloperidol instead of a second generation medication. He asked that the committee allow more than one of the three long-acting atypical injectable antipsychotics be on the PDL. Do not make the patient take Prolixin® or haloperidol long-acting injectable because of the risk of tardive dyskinesia. He stated an open formulary is needed for children and adolescents if not for the adults, though preferred, so the doctor can take into effect the efficacy and side effect profiles of the medication. If open access is not offered to children and adolescents, make available two or more FDA-approved second generation antipsychotics. He asked that the quality of life for these seriously mentally ill patients and their families be considered and the long-term adverse budget effects of restricting antipsychotic medications for the mentally ill.

Judy Britt asked for clarification regarding the review and inclusion of the long-acting antipsychotics on the PDL. Dave Wuest responded that they are not being reviewed as

part of this category today and there will be open access for the long-acting injectable agents.

Coleen Lawrence clarified grandfathering and a look back. She stated that a timeframe is not being suggested of when the patient had to have had the drug. A physician can provide documentation that the patient had previously been on the drug and there is no time limit for previous utilization. The look back period is looking at claims history in the pharmacy system for a set period of time.

Allen Wu, Ortho McNeil, asked for clarification if the long-acting injectables are all going to be available on the PDL. Rob Coppola replied that they are not being considered for the PDL; there will be unrestricted access.

John Brokars, Eli Lilly, spoke in support of olanzapine (Zyprexa®). There is a black box warning that elderly patients who have dementia-related psychosis are not indicated for olanzapine. Zyprexa® has demonstrated greater efficacy based on PANSS score as compared to Risperdal®, Seroquel®, Abilify® and Geodon®. A separate 150 study randomized control trial comparing first and second generation antipsychotics showed that Clozaril®, Risperdal® and Zyprexa® were more efficacious in the PANSS change than the first generation agents. In industry-related studies from this analysis, Risperdal® no longer remains more significantly efficacious than the first generation but Zyprexa® did. Zyprexa® use has been associated with greater adherence to medication therapy which is an important attribute to avoiding hospitalizations. Published in *The New England of Medicine*, Zyprexa's® favorable efficacy is also indicated by greater reduction in psychopathology; lower rate of hospitalizations as noted in the CATIE Study in 2005. Overall direct healthcare expenditures for olanzapine treated patients were comparable or lower to alternative treatments. These cost differences were driven primarily by lower inpatient stays. Zyprexa® has been shown to be cost-effective in several studies directly against quetiapine, risperidone and groups comparing first and second generation antipsychotics. Several Medicoids have attempted to restrict olanzapine and have not shown cost savings in the pharmacy budget or in total overall costs. The efficacy of Zyprexa® must be balanced with the risks. Side effects include a higher incidence of awakening in adolescence and children. Somnolence and dizziness are commonly associated with Zyprexa®. In some cases, there are ketoacidosis or hyperosmolar death. All atypical antipsychotics should be monitored for increases in hyperglycemia.

B. Drug Class Review Presentation – First Health Services

Rob Coppola thanked the public for their comments. He stated that the presentation and discussion of the second generation antipsychotics will include aripiprazole, clozapine, iloperidone, ziprasidone, paliperidone, risperidone, asenapine, quetiapine, and olanzapine. Clozapine is available in generic and brand; risperidone is also available in a generic formulation. Consideration of these agents will be for the oral agents; all dosage forms other than the injectables. All of the agents have an indication for schizophrenia in adults with the exception of Symbyax®. Abilify®, Zyprexa®, Risperdal® and Seroquel® are approved for use in patients aged thirteen to seventeen years old. Most also have an indication for bipolar disorder in adults including Seroquel®, Seroquel XR®, Symbyax® and Zyprexa® which, in addition, have an indication for use relating to depressive episodes related to bipolar disorders. Abilify®, Risperdal® and Seroquel® have approval for use in patients aged ten to seventeen years old; Zyprexa® has approval for use in patients thirteen to seventeen years of age. Abilify®, Geodon®, Seroquel®, Seroquel XR® and Zyprexa® have an indication for the maintenance treatment of bipolar disorder. Zyprexa®, Seroquel® and Seroquel XR® are indicated for use in depressive episodes relating to bipolar disorder. Abilify®, Zyprexa® and Seroquel XR® also have approval for adjunctive treatment of depression in adults. Abilify® (for patients six to seventeen years old) and Risperdal® (for patients five to sixteen years old) are approved for treatment of irritability associated with autistic disorder. Invega® has an additional approval for schizoaffective disorder. The atypicals have an increased affinity for

serotonin receptors compared with dopamine receptors when compared to typicals which should lead to less EPS and other dopamine related side effects. The basic pharmacology is Serotonin-dopamine antagonism. There is no evidence supporting activity at any given receptor that leads to resolution of any given symptom. There is evidence that receptor activity will determine the adverse event profile. Dr. Coppola presented a chart of receptor activity and side effects in addition to a breakdown based on the activity of these receptors with the major complications of this therapy. The range of complications is sedation, EPS, anticholinergic effects, orthostatic hypotension, weight gain/dyslipidemia/diabetes mellitus – or metabolic syndrome, and QT prolongation. He noted that clozapine and Zyprexa® have high metabolic syndrome risk, specifically, weight gain and the related effects. Clozapine and Seroquel® have a high sedation rate. EPS is higher with Risperdal® (above 6mg per day) and Geodon®. The newer agents have less clinical experience and effectiveness studies, at this time, and are not included in large scale studies such as CATIE. There are no clinically significant differences in the pharmacokinetics of these agents. Abilify® and Fanapt® have active metabolites with long half lives; Seroquel® and Risperdal® also have active metabolites. Most of these agents are dosed once per day; Saphris®, Seroquel® and Clozaril® are dosed more frequently. There are few clinically relevant drug interactions. In terms of contraindications, clozapine is contraindicated in patients with myeloproliferative disorders; uncontrolled epilepsy; and patients with a history of clozapine-induced agranulocytosis or severe granulocytopenia. Ziprasidone is contraindicated in patients with recent acute MI or uncompensated heart failure. All of the agents carry a black box warning for increased mortality in elderly patients with dementia-related psychosis. All have a risk of EPS, TD, NMS, and with some agents, there is a risk of QT prolongation. There is a risk of agranulocytosis with clozapine. Seroquel® use requires cataract monitoring and most of the agents require seizure monitoring. All agents are rated Pregnancy Category C with the exception of clozapine which is rated Category B. He referred to the breakdown of studies related to indications in the pediatric population included in the handout. Caution should be taken with clozapine and Seroquel® for patients with hepatic impairment and Saphris® should be avoided in these patients. For patients with renal impairment, Invega® dosing should be monitored or individualized. Studies indicate that patients of Jewish decent have shown a disproportionate number of cases of clozapine-related agranulocytosis. All of the agents within the class are first line agents in the treatment of schizophrenia and bipolar disorder. There is no evidence to suggest that one agent is clinically more efficacious than another and the drugs can be clinically differentiated primarily by their side effect profiles. There is limited data available through quality head-to-head trials, but indirect comparisons, meta-analysis and systematic reviews have demonstrated comparable efficacy, but that differences exist in their adverse event profiles. DHCFP and First Health recommend that in terms of efficacy, the agents in this class be considered therapeutic alternatives.

- C. Committee Discussion and Action to approve Clinical/Therapeutic Equivalency of Agents in Class and to Identify Exclusions/Exceptions for Certain Patient Groups

MOTION: Constance Kalinowski motioned that the agents in this class be considered therapeutic alternatives.

SECOND: Judy Britt

VOTES: Unanimous

MOTION CARRIED

- D. Presentation of Recommendations for Preferred Drug List (PDL) Inclusion by First Health Services and the Division of Health Care Financing and Policy

Rob Coppola stated that it is the recommendation of DHCFP and First Health that clozapine, Fanapt®, Geodon®, risperidone (all dosage forms), Seroquel® and Seroquel XR® are preferred. There are agents reflective in this list that minimizes the risk of the major event profiles of EPS, metabolic syndrome and sedation.

- E. Committee Discussion and Approval of Drugs for Inclusion on the PDL

Dr. Manthei asked why clozapine is being recommended since the risk for sedation, anticholinergic effects, orthostatic hypotension, weight gain, dyslipidemia and diabetes is high.

Rob Coppola responded that clozapine has a lower risk pregnancy category rating (clozapine is Pregnancy Category B; all others are Pregnancy Category C).

Judy Britt added that in her twenty-five years of experience in the mental health business, clozapine is the only atypical antipsychotic that truly is atypical in the sense that it's used for the resistant schizophrenia in which no other drug works. It was reserved for those mentally ill patients who did not respond to anything else and it changed their lives. Since then, there has been no other drug that has come close to giving the response for the resistant schizophrenic like this drug. When looking at a preferred drug list, it has to be on there to address the patients who absolutely do not respond to anything else.

Dr. Nagy asked if there are any specific drugs on the preferred list for pediatrics.

Rob Coppola replied that Risperdal® is approved for children down to five years of age, Abilify at six years for irritability related to autistic disorder; and all of the other agents have comparable indications in pediatrics.

MOTION: Constance Kalinowski motioned to accept First Health's recommendation that clozapine, Fanapt®, Geodon®, risperidone (all dosage forms), Seroquel® and Seroquel XR® be on the PDL.

SECOND: Shamim Nagy

Chad Luebke commented that Abilify® and Invega® are better in terms of the side effect profile, particularly Abilify®, and asked why it is not being included. Dr. Coppola responded that Invega® is a newer drug with not much experience or data available in his opinion and in terms of Abilify®, there is no way to look at a patient and be able to predict how they are going to respond to a drug whether it be the adverse event profile or efficacy. Based on that, it would seem reasonable to have a trial of one of the proposed agents first.

Dr. Kalinowski added that in practice, Geodon® and Abilify® are thought of as being the two antipsychotics that one would use preferentially for someone who comes in with pre-existing metabolic syndrome or weight issues and these two agents are seen as comparable.

AYES: Holt, Chan, Hautekeet, Havins, Manthei, Nagy, Kalinowski, Britt

NAYES: Luebke

MOTION CARRIED

Coleen Lawrence clarified that the State will act in accordance with SB4 and will be grandfathering this class of drugs.

Dave Wuest commented that there are two types of look backs. There is the automatic look back where the system looks through the history of claims received and will automatically process an incoming claim if there is a history of a paid claim for that drug; no PA is required.

Coleen Lawrence added that this type of look back is typically ninety days. Ninety days has been the maximum for most claims history look backs. There are some drugs that have a thirty day look back in history. The look back period is determined by the committee.

Dave Wuest stated that the other type of look back is that the medical history, outside of the drug claim file, indicates that there was a trial and failure or trial and allergy, etc., which can be communicated by the prescriber to the Clinical Call Center for prior authorization.

Chad Luebke said that with any prior use, wouldn't it make sense to have the system look back as far as possible.

Coleen Lawrence responded that a complicated look back system will result in a system error at the pharmacy, causing the claim to time out, requiring the pharmacy to resubmit the claim. There are system limitations and the ninety day mark is a safe look back period. In addition, a physician can follow the prior authorization process by calling the Clinical Call Center and the PDL exception criteria can be applied to medication history beyond the ninety days.

VIII. Report by FHSC on New Drugs to Market, New Generic Drugs to Market, and New Line Extensions

Paula Townsend reviewed the PDL Revisions Report included in the meeting binder.

IX. Review of Next Meeting Location, Date, and Time

The next meeting is scheduled for June 24, 2010. The meeting will be held in southern Nevada at the Las Vegas Chamber of Commerce with videoconferencing to the northern Nevada location which will be held at the First Health Services office in Reno. Public seating at First Health Services is limited.

Ms. Lawrence added that due to the State's budget restrictions, there are no travel funds available. The P&T and DUR Board meetings will be videoconferenced between northern and southern Nevada for the remainder of the year. Due to limited seating, the First Health site will only hold approximately ten of the public.

X. Public Comment

No comment.

XI. Adjournment

MOTION: Justin Holt motioned to adjourn the meeting.

SECOND: Chad Luebke

VOTES: Unanimous

Meeting adjourned at 2:55p.m.